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Complex Formation of Perfumes with Cationic Surfactants and the Enhanced Thermal Stability

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Seven crystalline molecular complexes were formed between perfumes such as guaiacol, 2-methylindole, and skatole and cationic surfactants such as hexadecyl-, tetradecyl-, dodecyl-, and decyltrimethylammonium bromide from an aqueous or methanol solution at low temperatures (< 10 °C). The crystal structures were determined by X-rays. The structures are very similar to each other, that is, the perfume molecules are packed in the layers of the alkyl chains of the surfactant molecules. Those packings are substantially the same as the common packing pattern observed in complexes between the surfactants and the aromatic compounds. The thermal analysis showed that the volatilization temperatures of the perfumes increased significantly when the perfumes are packed in the complex crystals. Moreover, the molar loss ratio of the perfume with increasing the temperature decreased with increasing the length of the alkyl chain of the surfactant. This suggests that thermal stability of the perfumes can be controlled by forming the complexes with the surfactants containing different alkyl chains.

The ionic surfactants such as quaternary ammonium salts form spherical micelles in aqueous solutions at concentrations above a critical micelle concentration (cmc).[1] If some aromatic compounds are added in the aqueous solution containing the surfactant, they are solubilized and the solution shows high viscoelasticity.[2—4] Some gigantic micelles were observed by electron microscopy.[5—8] From the solution containing a cationic surfactant such as hexadecyl-, tetradecyl-, dodecyl-, or decyltrimethyl-ammonium bromide (abbreviated as CTAB, MTAB, LTAB, and DTAB, respectively) and several aromatic substances such as various phenolic derivatives or basic substances, a variety of crystalline molecular complexes were obtained at low temperatures.[9—11] The crystal structure analysis by X-ray diffraction indicated that the packing patterns of the surfactant and aromatic molecules in the crystals are very similar to each other; this is called a "common packing pattern".[12] This suggested that unstable drug molecules may be packed and stabilized by the surfactant molecules to form crystalline molecular complexes. In the previous paper, the crystal structures of three molecular complexes between the drug molecules such as 1-(2,4,6-trihydroxyphenyl)-1-propanone (flopropione) or 4-chloro-*m*-cresol and the surfactants such as CTAB or MTAB were analyzed by X-rays. The common packing pattern observed in the three crystals well explained the results of the thermal analyses that the drug molecule in the molecular complex is more stable thermally than that in the pure form.[13]

Recently we intended to form molecular complexes between the cationic surfactants and the perfumes to delay volatilization of the perfumes. After many trials, it was formed that the perfumes such as 2-Methylindole, Skatole, and Guaiacol formed crystalline molecular complexes with the cationic surfactants such as CTAB, MTAB, LTAB, and DTAB. The crystals suitable for X-ray analysis were obtained for the seven complexes between 2-methylindole and CTAB, MTAB, and LTAB, (**I**, **II**, and **III**, respectively), and between skatole and CTAB, MTAB, and LTAB, (**IV**, **V**, and **VI**, respectively), and between CTAB and guaiacol, (**VII**). This paper reports the structures of the seven crystals analyzed by X-rays and the enhanced thermal stability.

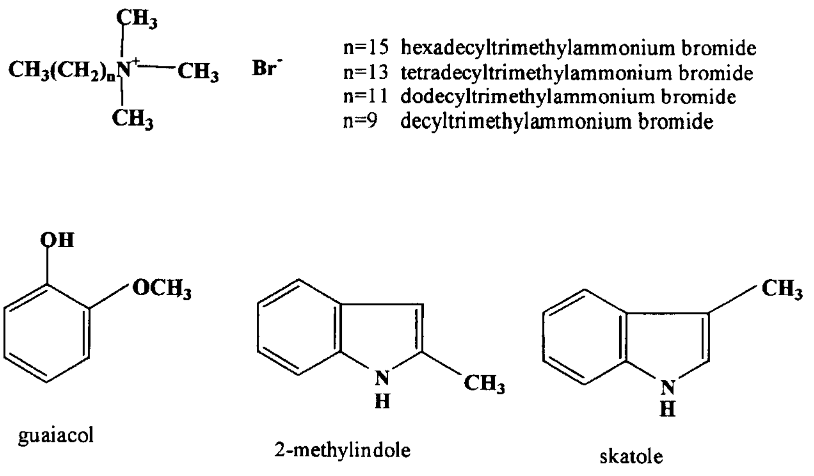
Experimental

Preparation of the Complex Crystals. Cationic surfactants of CTAB, MTAB, and LTAB were crystallized from methanol–acetone solutions and then recrystallized from aqueous solutions. The perfumes of 2-methylindole and skatole were purchased from Tokyo Kasei Co., Ltd. and were purified by a conventional recrystallization. The structural formulae of the surfactants and perfumes are shown in the Scheme 1. The perfume of 2-methylindole or skatole and the cationic surfactant, CTAB, MTAB or LTAB were dissolved in a methanol solution in a molar ratio of 1 : 1. The solution was kept in a refrigerator at lower than 10 °C. Plate-like crystals **I**—**VI** suitable for X-ray studies were obtained after a week. The complex crystals between Guaiacol and CTAB were obtained from an aqueous solubilized solution. The complex crystals of DTAB with the above perfumes and those of guaiacol with the cationic surfactants other than CTAB suitable for X-ray studies have not been obtained yet.

Crystal Structure Analysis. The crystal data and experimental details are summarized in Table 1. The crystal was mounted on the SMART-CCD diffractometer using Mo *Kα* radiation. The

Table 1. Crystal Data and Experimental Details

	I	II	III	IV	V	VI	VII
Formula	$C_{19}H_{42}NBr$ /$0.5C_9H_9N$	$C_{17}H_{38}NBr$ /$0.5C_9H_9N$	$C_{15}H_{34}NBr$ /$0.5C_9H_9N$	$C_{19}H_{42}NBr$ /$0.5C_9H_9N$	$C_{17}H_{38}NBr$ /$0.5C_9H_9N$	$C_{15}H_{34}NBr$ /$0.5C_9H_9N$	$C_{19}H_{42}NBr$ /$0.5C_7H_8O_2$
Molecular weight	430.03	401.98	373.93	430.03	401.98	373.93	426.51
Temperature/K	223	223	223	223	223	223	223
Wavelength/Å	0.71069	0.71069	0.71069	0.71069	0.71069	0.71069	0.71069
Diffractometer	SMART-CCD	SMART-CCD	SMART-CCD	SMART-CCD	SMART-CCD	SMART-CCD	SMART-CCD
Radiation	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1$	$P2_1$	$P2_1$	$P2_1$	$P2_1$	$P2_1$
a/Å	5.5160(16)	5.5240(1)	5.5400(1)	5.4943(3)	5.5092(12)	5.5072(2)	5.5123(2)
b/Å	7.4290(14)	7.4240(1)	7.4173(2)	7.4105(4)	7.395(2)	7.3926(2)	7.4272(3)
c/Å	31.680(6)	29.5280(2)	27.3813(3)	32.3954(19)	30.204(6)	27.9224(7)	32.4438(14)
α/°	90	90	90	90	90	90	90
β/°	90.449(11)	92.879(1)	95.786(1)	92.313(1)	94.325(18)	94.068(1)	92.247(1)
γ/°	90	90	90	90	90	90	90
Z	2	2	2	2	2	2	2
Volume/Å^3	1298.2(5)	1209.42(3)	1119.42(4)	1317.92(13)	1227.0(5)	1133.93(6)	1327.26(9)
D_{calc}/g cm^{-3}	1.100	1.104	1.109	1.084	1.088	1.095	1.067
Crystal dimensions/mm^3	0.25 × 0.25 × 0.10	0.30 × 0.20 × 0.10	0.30 × 0.20 × 0.08	0.25 × 0.25 × 0.20	0.22 × 0.20 × 0.08	0.20 × 0.20 × 0.10	0.30 × 0.30 × 0.05
Absorption correction	SADABS	SADABS	SADABS	SADABS	SADABS	SADABS	SADABS
$2\theta_{max}$/°	55	55	55	55	55	55	55
μ/mm^{-1}	1.591	1.704	1.836	1.567	1.679	1.813	1.558
F(000)	466	434	402	466	434	402	462
Range of h	$-6 \rightarrow 7$	$-7 \rightarrow 6$	$-6 \rightarrow 7$	$-6 \rightarrow 7$	$-7 \rightarrow 7$	$-7 \rightarrow 7$	$-6 \rightarrow 5$
Range of k	$-9 \rightarrow 9$	$-9 \rightarrow 9$	$-9 \rightarrow 9$	$-9 \rightarrow 9$	$-9 \rightarrow 8$	$-9 \rightarrow 9$	$-8 \rightarrow 7$
Range of l	$-42 \rightarrow 38$	$-38 \rightarrow 38$	$-35 \rightarrow 32$	$-34 \rightarrow 42$	$-34 \rightarrow 39$	$-28 \rightarrow 36$	$-35 \rightarrow 32$
No. of observed reflections Total	9860	12612	7947	7507	8687	8047	6987
Unique	6026	5207	4699	4601	4633	4882	3585
No. of refined parameters	271	205	228	255	270	237	262
R (int)	0.017	0.023	0.018	0.017	0.022	0.015	0.032
R ($I > 2\sigma$)	0.048	0.046	0.042	0.060	0.060	0.059	0.048
$wR(F^2)$	0.125	0.135	0.123	0.166	0.152	0.152	0.154
Goodness-of-fit on F^2	1.129	1.088	1.057	1.070	1.069	1.106	1.086
Weighting parameters							
a	0.0676	0.0864	0.0835	0.1003	0.0685	0.0617	0.1221
b	0.86	0.88	0.48	1.68	2.74	2.63	0
$\delta\rho$/e Å^{-3}	+0.93, −0.52	+1.19, −0.46	+1.07, −0.46	+1.92, −1.57	+1.78, −1.82	+2.31, −1.52	+0.98, −0.59



Scheme 1. Surfactant and perfume molecules.

temperature was cooled down to −50 °C with the cold nitrogen-gas-flow method. The structure was solved by the direct method with the program SIR-92,[14] and was refined by the full-matrix least-squares method with the program SHELX97.[15] The data collection and refinement methods were nearly the same for the seven crystals. All the crystals have the same space group, $P2_1$, and the structures are isostructural to each other. Since the molar ratio of the surfactant and the perfume is 2 : 1 in each crystal, the *a* axis length should be doubled. This means the unit cell has four surfactants and two perfumes in each crystal. Since the reflections with h = odd in the double cell have no significant intensities, a half cell along the *a* axis was taken. This means the crystal structure is an average between the two structures distributed at random along the *a* axis. In the refinements of all the crystals, the perfume molecules are disordered in the columns composed of the alkyl chains of the surfactant molecules and the bromide anions, although the surfactant molecules are ordered. The disordered perfume molecules were refined with the isotropic temperature factors and the ordered surfactant molecules were refined with the anisotropic temperature factors. Moreover, the C–C bonds and C–C–C angles of aromatic rings were constrained to 1.39 Å and 120 °, respectively. The C–O bond of guaiacol was constrained to 1.362 Å. The exocyclic C–CH_3

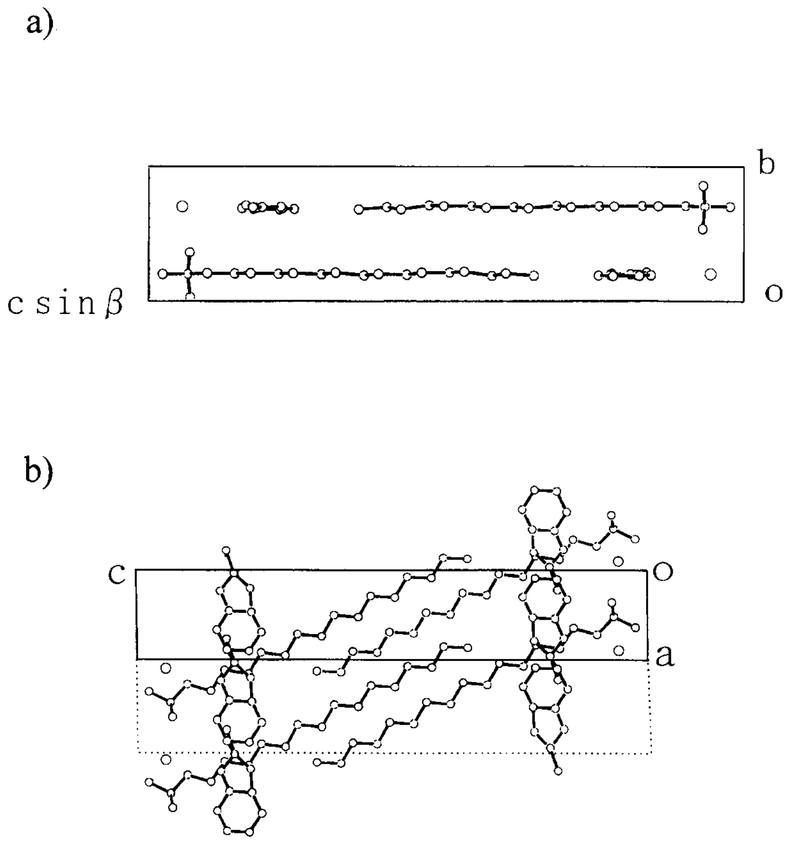


Fig. 1. Crystal structures of CTAB/2-methylindole (I) viewed along; a) the *a* axis and b) the *b* axis. The dotted line indicates the double cell along the *a* axis.

bond of 2-methylindole and skatole was constrained to 1.506 Å. The positions of the hydrogen atom were calculated and fixed in the refinement. Atomic scattering factors were taken from International Tables for Crystallography.[16] The weighting scheme applied to all the crystals is $1/[\sigma^2(F_o^2)+(aP)^2+bP]$ where $P = (F_o{}^2+2F_c{}^2)/3$. The CIF data for the seven crystals are deposited as Document No. 73020 at the Office of the Editor of Bull. Chem. Soc. Jpn. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 140730-140736.

Thermal Stability of the Complexes. Themogravimetry was carried out with a Rigaku TG8120 under nitrogen-gas-flowing condition at the heating rate of 10 °C min^{-1} in 25—160 °C range.

Results and Discussion

Crystal and Molecular Structure of CTAB/2-Methylindole (I). The crystal structures viewed along the *a* and *b* axes are shown in Fig. 1. Since the molar ratio of CTAB and 2-methylindole is 2 : 1, the *a* axis should be twice as shown in dotted line. In the double cell, there are two 2-methylindole molecules, which occupy two of the four molecular sites. This means the 2-methylindole molecules occupy alternately but at random along the *a* axis. Since there are rather loose contacts between the 2-methylindole molecules along the *a* axis, the 2-methylindole molecule takes four disordered structures (A, B, C, and D), the occupancy factors of which are 0.37, 0.23, 0.12, and 0.28 for A, B, C, and D, respectively. Only the A molecule is shown in Fig. 1. The molecular structures of CTAB and 2-methylindole A with the numbering of the atoms are shown in Fig. 2. The alkyl group of the surfactant takes an all-*trans* conformation. The N–H group of 2-methylindole makes a hydrogen bond with the bromide anion, N2A···Br1, 3.39(1) Å.

The aromatic ring of 2-methylindole is sandwiched by the alkyl chains of CTAB, which is similar to the "common packing pattern" as observed in the complex crystals between CTAB and aromatic compounds. Slightly short contacts are observed between the alkyl group of CTAB and the ring carbons of 2-methylindole, which may be C–H···π interactions as suggested by Sawada.[17] Similar packing patterns were observed in the other six complex crystals **II**—**VII**, since all the complex crystals are isostructural.

Crystal and Molecular Structures of MTAB/2-Methylindole (II) and LTAB/2-Methylindole (III). The crystal structures of **II** and **III** viewed along the *b* axis are shown in Figs. 3(a) and 3(b), respectively. The molecular structures of **II** and **III** with the numbering of the atoms are shown in Figs. 4(a) and 4(b), respectively. The structures are substantially the same as that of **I** except for the differences in length of the alkyl chains of the surfactant molecules. The 2-methylindole molecule in **II** is disordered with two orientations A and B. The occupancy factors converged to 0.62 and 0.38 for A and B, respectively. On the other hand, the 2-methylindole molecule in **III** is disordered with four orientations (A, B, C, and D). The occupancy factors are 0.53, 0.12, 0.18, and 0.17 for A, B, C, and D, respectively. Only the A molecules of **II** and **III** are drawn in Figs. 3 and 4. The N–H group of 2-methylindole in **II** or **III** makes a hydrogen bond with the bromide anion. The distances of N2A···Br1 for **II** and **III** are 3.52(2) and 3.49(6) Å, respectively.

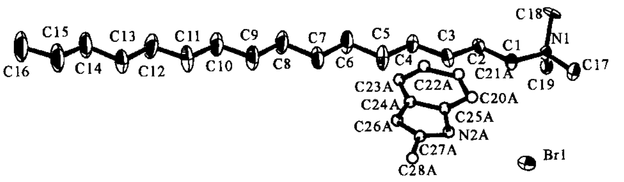


Fig. 2. Molecular structure of CTAB/2-methylindole (I) showing 50% thermal ellipsoids and the atomic numbering. Only the major orientation A of 2-methylindole is shown.

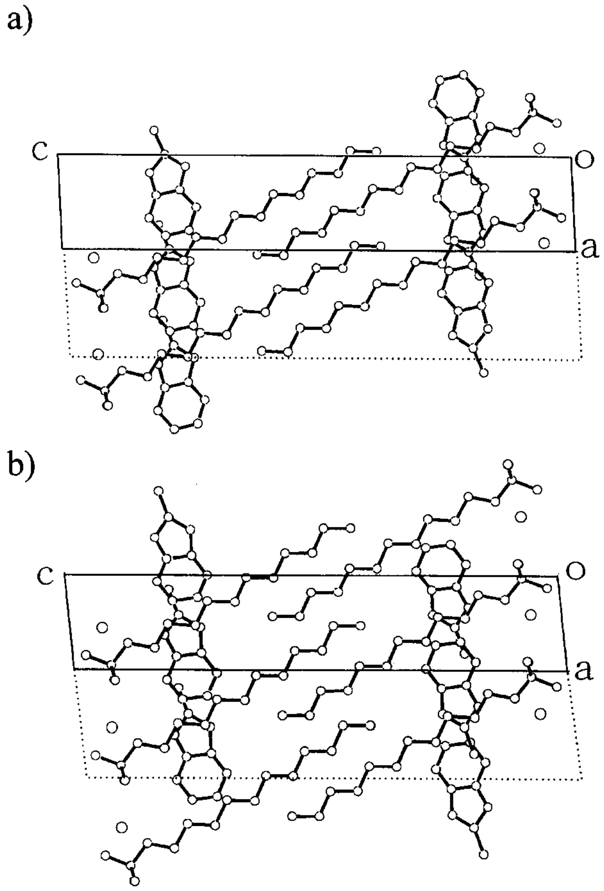


Fig. 3. Crystal structures of; a) MTAB/2-methylindole (**II**) and b) LTAB/2-methylindole (**III**) viewed along the *b* axis.

Crystal and Molecular Structures of CTAB/Skatole (IV), MTAB/Skatole (V), and LTAB/Skatole (VI). The crystal structure of **IV** viewed along the *b* axis is shown in Fig. 5. The crystal structures of **V** and **VI** are very similar to that of **IV** except that the alkyl chains of **V** and **VI** are shorter than that of **IV**. The molecular structures of **IV**, **V**, and **VI** with the numbering of the atoms are shown in Fig. 6. In the three crystals, the alkyl groups of the surfactant molecules take an all-*trans* conformation. The skatole molecules take disordered structures in the columns surrounded by the surfactant molecules in all three crystals. The skatole molecule

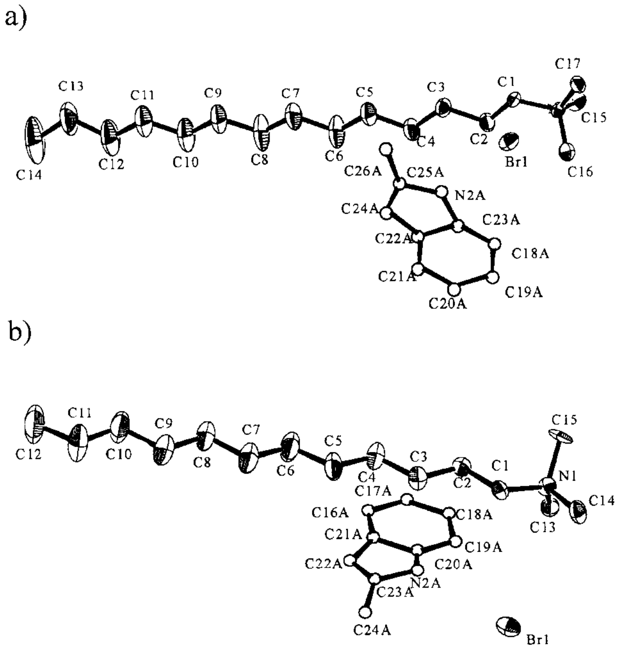


Fig. 4. Molecular structures of; a) MTAB/2-methylindole (**II**) and b) LTAB/2-methylindole (**III**) showing 50% thermal ellipsoids and the atomic numbering.

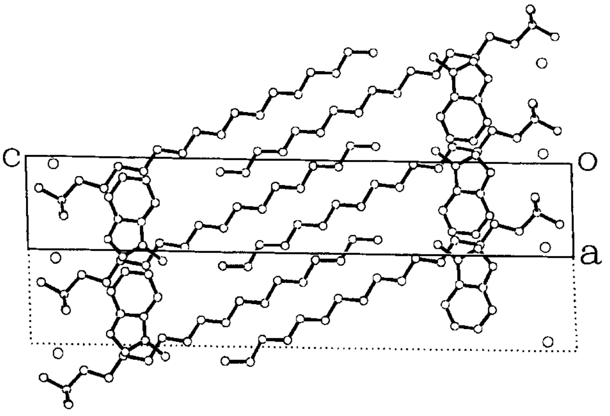


Fig. 5. Crystal structure of CTAB/skatole (**IV**) viewed along the *b* axis.

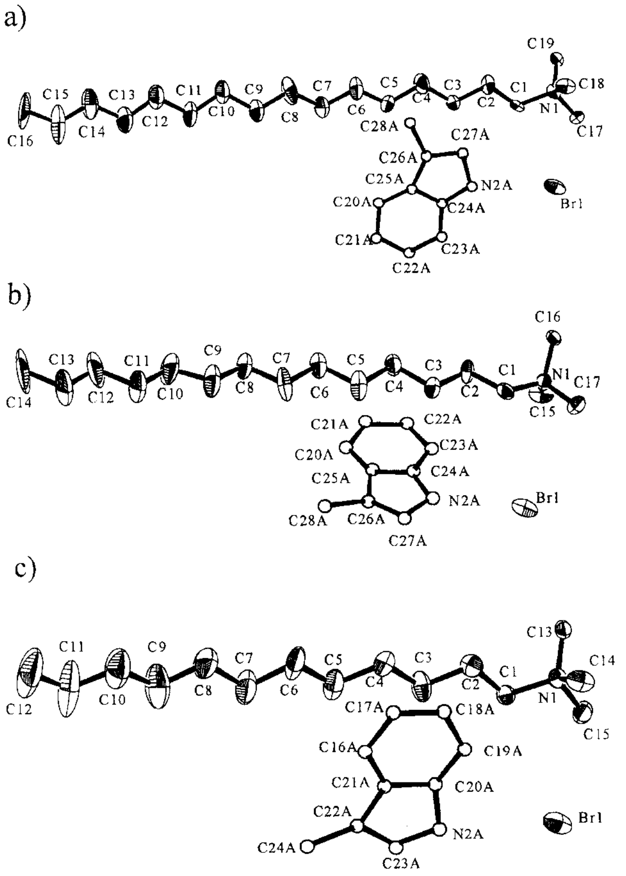


Fig. 6. Molecular structures of; a) CTAB/skatole (**IV**), b) MTAB/skatole (**V**), and c) LTAB/skatole (**VI**) showing 50% thermal ellipsoids and the atomic numbering.

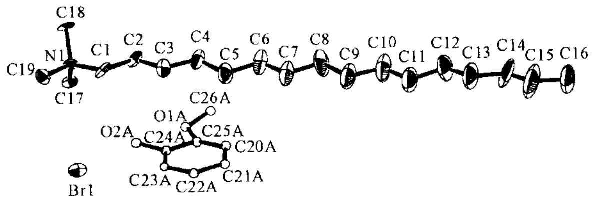


Fig. 7. Molecular structures of CTAB/guaiacol (**VII**) showing 50% thermal ellipsoids and the atomic numbering.

in **IV** has three orientations (A, B, and C), whereas those in **V** and **VI** have five and four orientations. The occupancy factors are 0.35, 0.25, 0.32, and 0.08 for A, B, C, and D of **IV**, 0.34, 0.30, 0.14, 0.14, and 0.09 for A, B, C, D, and E of **V**, and 0.42, 0.22, 0.22, and 0.14 for A, B, C, and D of **VI**. In each crystal, the N–H group of skatole makes a hydrogen bond with the bromide anion. The distances of N2A···Br1 are 3.30(2), 3.32(2), 3.45(28) Å for **IV**, **V**, and **VI**, respectively.

Crystal and Molecular Structure of CTAB/Guaiacol (VI). The crystal structure is nearly the same as those of **I** and **IV** except that guaiacol occupies the disordered positions in the column surrounded by surfactant molecules instead of 2-methylindole or skatole. The molecular structure with the numbering of the atoms is shown in Fig. 7. The disordered guaiacol molecule has four orientations (A, B, C, and D). The occupancy factors of A, B, C, and D are 0.31, 0.24, 0.21, and 0.24, respectively. The O–H group of guaiacol makes a hydrogen bond with the bromide anion. The distance of O2A···Br1 is 3.02(2) Å.

Thermal Stability of the Complex Crystals. The thermogravimetry of 2-methylindole and the three molecular complex crystals between 2-methylindole and CTAB, MTAB, and LTAB are shown in Fig. 8. Although the volatilization of 2-methylindole begins at about 70 °C not only in pure crystal but also in the complex crystals, the volatilization rate of the pure crystal is significantly greater than that of the complex crystals. Moreover, as the length of the alkyl chain increases, the rate of volatilization decreases.

Figure 9 shows the ratio of molar loss of skatole with increasing temperature for the pure crystal and the four molecular complexes with CTAB, MTAB, LTAB, and DTAB. The

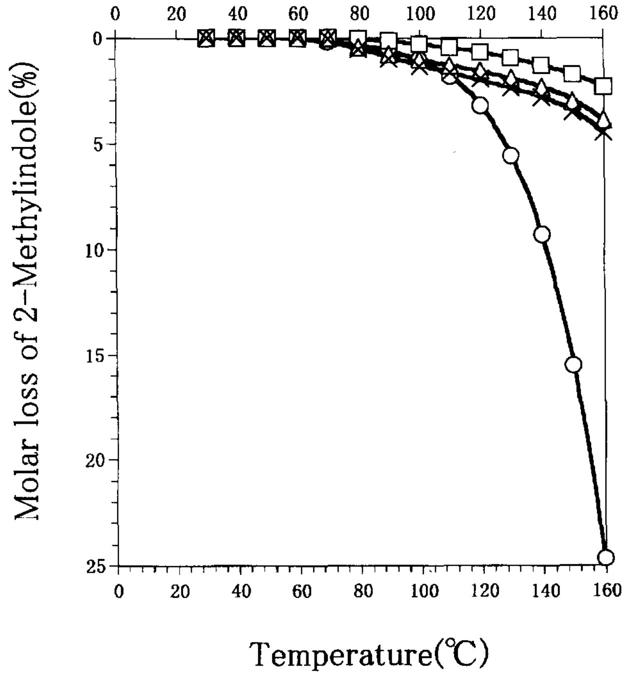


Fig. 8. Molar loss of 2-methylindole with temperature in the complex crystals with CTAB (-□-), MTAB (-△-), and LTAB (-×-) compared with the pure crystal of 2-methylindole (-○-).

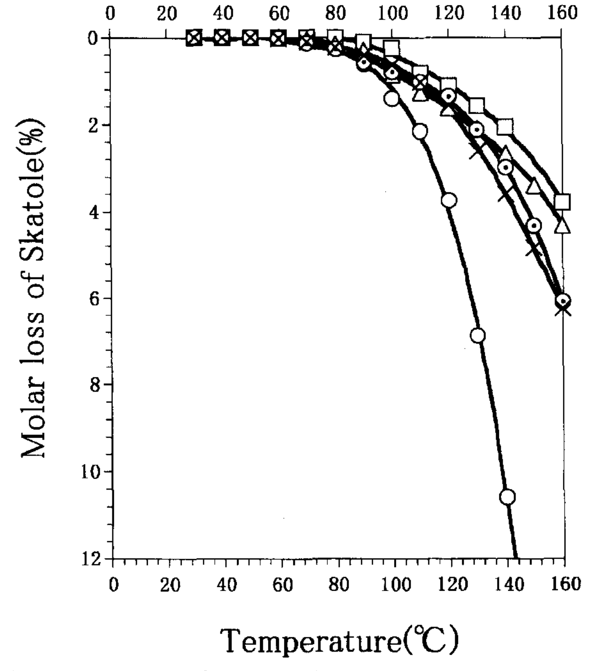


Fig. 9. Molar loss of skatole with temperature in the complex crystals with CTAB (-□-), MTAB (-△-), LTAB (-⊙-), and DTAB (-×-) compared with the pure crystal of skatole (-○-).

volatilization of skatole begins at about 70 °C but the rate of volatilization of skatole in pure crystal is significantly greater than those in the complex crystals. Moreover, the rates of volatilization of skatole are significantly greater than the corresponding ones of 2-methylindole, although the volatilization of skatole begins at nearly the same temperature as that of 2-methylindole. The above results indicate that the perfumes are more stable in the molecular complexes than in pure crystal and that the stability depends on the alkyl chain lengths of the surfactants.

Table 2. The van der Waals Energies (V_{ij}) for the Complex Crystals Using the Lennard–Jones Potential

	V_{ij}/kJ mol^{-1}
CTAB/2-Methylindole	−4.155
MTAB/2-Methylindole	−3.265
LTAB/2-Methylindole	−2.429
CTAB/Skatole	−3.858
MTAB/Skatole	−3.041
LTAB/Skatole	−2.215

In order to explain the stability on the basis of the crystal structure, the van der Waals energy for each molecular complex was calculated using the Lennard–Jones potential.[18] Only the C···C interactions less than 5 Å between the neighboring alkyl groups were taken into account in the first approximation, since the positions of the hydrogen atoms of the alkyl group were obtained geometrically from the positions of the carbon atoms. Moreover, the electrostatic energy may be approximately the same, since the ammonium cation and bromide anion occupy nearly the same position in each crystal. Table 2 shows the van der Waals energies for the complex crystals between 2-methylindole or skatole and CTAB, MTAB, or LTAB. As the length of the alkyl chain decreases, the numbers of the contacts less than 5 Å decrease, as shown in Figs. 1 and 3. This causes the increase in van der Waals energy as the alkyl group is shorter, which is clearly shown in Table 2. The van der Waals energy of each 2-methylindole complex is lower than the corresponding one of the skatole complex. This is the reason why the rates of volatilization of skatole are significantly greater than the corresponding ones of 2-methylindole, although the volatilization of skatole begins at nearly the same temperature as that of 2-methylindole.

In summary, the complex formation of the perfume with the surfactant decreases the volatilization rate of the perfume and the rate can be controlled by the length of the alkyl group of the surfactant.

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